

In the Claims

Please cancel claims 3, 4, 9, 16-20, 22, 23, 26-28, 38, 39, 42 and 47 and please amend the claims as shown below.

New claim 49 is presented.

1. (Currently amended) A DNA construct comprising a transcriptional unit which comprises a ribonucleotide reductase gene ~~and thioredoxin gene or a uridine kinase gene and/or a dCTP deaminase gene~~, wherein the ribonucleotide reductase gene comprises a T4 nrdA gene modified to comprise SEQ ID No. 9.

2. (Currently amended) A DNA construct as claimed in claim 1 comprising a transcriptional unit further comprising a T4 nrdB gene and a thioredoxin gene wherein the thioredoxin gene is a T4 nrdC gene.

3. – 4. (Canceled)

5. (Currently amended) A DNA construct according to claim 4 2 wherein the construct is ~~an extrachromosomal~~ a vector.

6. (Currently amended) A DNA construct according to claim 5 wherein the vector is a ~~plasmid~~, virus, transposon, minichromosome or phage.

7. (Currently amended) A DNA construct according to claim 6 wherein the vector is a plasmid, and wherein the ~~ribonucleotide reductase gene is a modified T4 nrdA gene, and/or a the T4 nrdB gene, and wherein the thioredoxin gene is a the T4 nrdC gene and said genes~~ are arranged in an operon.

8. (Currently amended) A DNA construct according to claim 7 wherein the transcriptional unit comprises ~~a the modified T4 nrdA gene and a~~

the *nrdB* gene, and wherein the modified T4 *nrdA* and T4 *nrdB* genes are located downstream of the T4 *nrdC* gene.

9. (Canceled)

10. (Currently amended) A DNA construct according to claim 8 wherein the T4 *nrdC* gene is upstream of the modified T4 *nrdA* gene and the modified T4 *nrdA* gene is upstream of the T4 *nrdB* gene.

11. (Original) A DNA construct according to claim 6, further comprising a regulatory element.

12. (Original) A DNA construct according to claim 11, wherein the regulatory element is selected from the group consisting of a promoter, an operator, a termination sequence, an initiation sequence and a ribosome binding site.

13. (Original) A DNA construct according to claim 12 wherein the promoter is the lambda P_L promoter or a derivative therefrom.

14. (Currently amended) A DNA construct according to claim 12 wherein the termination sequence is a synthetic heterologous terminator sequence.

15. (Currently amended) A DNA construct according to claim 7 1 wherein the modified T4 *nrdA* gene is modified such that ribonucleotide reductase encoded by the unit is less sensitive to allosteric inhibition than the wild type equivalent of said ribonucleotide reductase encoded by the unit comprising an unmodified *nrdA* gene.

16. – 20. (Canceled)

21. A DNA construct according to ~~any of claims 1-4~~ claim 1 wherein the construct further comprises a ~~thymidylate synthase~~ T4 td gene.

22. – 23. (Canceled)

24. (Currently amended) A DNA construct according to claim ~~22~~ 21 wherein the *td* gene is located in the same operon as the *nrdA*, *nrdB* and *nrdC* genes.

25. (Currently amended) A DNA construct according to claim 24 wherein *td* gene is located downstream ~~(in terms of reading frame)~~ from the modified *nrdA*, *nrdB* and *nrdC* genes.

26. – 28. (Canceled)

29. (Currently amended) A DNA construct according to claim 2 further comprising ~~a~~ an *E.coli* uridine kinase gene ~~and/or a~~ an *E. coli* dCTP deaminase gene.

30. (Currently amended) A DNA construct according to claim 29, wherein the DNA construct comprises both ~~a~~ an *E.coli* uridine kinase gene and ~~a~~ an *E.coli* dCTP deaminase gene.

31. (Currently amended) (Previously amended) A DNA construct according to claim 1 wherein the *E.coli* uridine kinase gene is a *udk* gene. 3, 4, 9, 16-20, 22, 23, 26-28, 38, 39, 42 and 47

32. (Currently amended) (Previously amended) A DNA construct according to claim ~~4-30~~ wherein the *E.coli* dCTP deaminase gene is a *dcd* gene

33. (Currently amended) A modified E.coli host cell comprising a DNA construct according to any one of the preceding claims 1, 2, 5-8, 10-15, 21, 24, 25, 29-32.

34. (Currently amended) A modified E.coli host cell according to claim 33 wherein the host cell displays repressed or no uracil DNA glycosylase activity.

35. (Currently amended) A modified E. coli host cell according to claim 34 wherein one or more host cell DNA-sequences polynucleotides encoding for uracil DNA glycosylase activity have been modified so as to encode expression products displaying repressed, low levels of, or no uracil DNA glycosylase activity.

36. (Currently amended) A modified E.coli host cell according to claim 35 wherein the modified host cell DNA polynucleotides comprises sequence is an ung gene.

37. (Currently amended) A modified E.coli host cell according to claim 34 wherein one or more host cell DNA polynucleotides sequences encoding for uracil DNA glycosylase activity have been removed.

38. – 39. (Canceled)

40. (Currently amended) A modified E.coli host cell comprising a DNA construct, which construct comprises a transcription DNA unit, which unit comprises a modified T4 nrdA gene modified T4 nrdA gene comprising SEQ ID No 9 and a T4 nrdB gene encoding a ribonucleotide reductase and a thioredoxin- T4 nrdC gene, wherein said ribonucleotide reductase displays less sensitivity to allosteric inhibition than the wild-type equivalent of the reductase, and wherein said host cell further comprises one or more of the following features:

- (a) a transcription unit located on said DNA construct, comprising a thymidylate synthase gene heterologous to the thymidylate synthase gene of the host cell;
- (b) a transcription unit located on said DNA construct, comprising a an E. coli uridine kinase gene;
- (c) a transcription unit located on said DNA construct, comprising a an E. coli dCTP deaminase gene; and
- (d) repressed or absent uracil DNA glycosylase activity.

41. (Currently amended) A modified E.coli host cell according to claim 40, wherein the ribonucleotide reductase gene is modified at a dTTP binding site.

42. (Canceled)

43. (Currently amended) A modified E.coli host cell according to claim 38 40, wherein the DNA construct comprises both the uridine kinase gene and the dCTP deaminase gene.

44. (Currently amended) A modified E.coli host cell according to claim 40, wherein the cell comprises each one of the features of (a) to (d).

45. (Previously amended) A process for the production of pyrimidine deoxyribonucleosides comprising culturing a host cell according to claim 33.

46. (Original) A process according to claim 45 wherein the deoxyribonucleoside is thymidine.

47. (Canceled)

48. (Previously amended) A culture medium comprising a host cell according claim 33.

49 (New) A DNA construct comprising a transcriptional unit which comprises a ribonucleotide reductase gene, wherein the ribonucleotide reductase gene comprises a T4 *nrdA* gene modified at a dTTP binding site such that ribonucleotide reductase encoded by the unit is less sensitive to allosteric inhibition than the wild type equivalent of said ribonucleotide reductase encoded by the unit comprising an unmodified *nrdA* gene.